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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SMITH, CAROLYN L	

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 04/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/723,256	DUNLAY ET AL.	
	Examiner	Art Unit	
	Carolyn L Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *30,44,54 and 61-65* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30, 44, 54, 61-65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/23/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicants' amendments and remarks, filed 1/23/04, are acknowledged. Amended claims 30, 44, 54, and 64 are acknowledged.

Applicant's arguments, filed 1/23/04, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from the previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The information disclosure statement, filed 1/23/04, has been considered by the Examiner.

Claims 30, 44, 54, and 61-65 are herein under examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30, 44, 54, and 61-65 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This rejection is necessitated by amendment.

Consideration of the support pointed to by Applicants regarding amending the claims to cite "plasma" membrane instead of cell membrane on pages 68-70 reveals that this amendment is NEW MATTER. No masking is cited on page 68. On page 69, lines 11-14, images of probes used to mark the "plasma membrane and cytoplasm" are used to mask the image.... This supports a mask that is inclusive of both the plasma membrane and cytoplasm. No separate mask is cited such as now present in the amended claims. On page 70, lines 15-18, similarly a masking of both plasma membrane and cytoplasm again is cited. No separate plasma membrane versus cytoplasm masking has written support. The amendment to the claims; such as claim 30; parts d), e), and f); cite the phrase "plasma membrane mask and the cell membrane mask". This indicates separate masks that is not what pages 68-70 supply written basis for. Because the introduction of "plasma" in amended claims 30, 54, and 64, filed 1/23/04, lack written support, phrases including this term as described above are considered NEW MATTER. This rejection is necessitated by amendment.

Claim Rejections – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. (e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 30, 44, 54, and 61-65 is maintained under 35 U.S.C. 103(a) as being unpatentable over Cabib et al. (P/N 5,784,162) in view of *In re Venner* (262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958)).

This rejection is maintained and reiterated for reasons of record.

Cabib et al. describe bio-imaging methods involving measurements and analysis software that detect spatial organization, such as distribution, and quantify cellular constituents, structures, organelles and administered components such as tagged fluorescent probes and drugs (test stimulus) using light transmission, reflection, scattering, and fluorescence emission strategies (col. 1, lines 13-25 and col. 2, lines 3-4). Cabib et al. describe using the method for cell and tissue classification, in drug development research as well as mapping cytoplasm organelles and constituents and the cell membrane (col. 10, line 62 to col. 11, line 12 and col. 38, line 17 to col. 39, line 9). Cabib et al. describe algorithms to interpret spectral information of chemical elements (concentration mapping) and/or morphological interpretation using image shapes (col. 61, lines 33-45). Cabib et al. describe using the cell, tissue or organism samples to monitor life

processes in the sample as a function of time (col. 11, lines 30-34). Cabib et al. describe scanning of multiple cells in an array of locations using an image spectrometer as seen in Figure 1 (col. 16, lines 36-67). Cabib et al. describe measuring spatial separation between at least two fluorophores where one is administered to the sample (col. 11, lines 13-18). Cabib et al. describe using spectral imaging to detect proteins and nucleic acid sequences after being labeled with fluorescent probes, mapping, and sorting out several fluorophores in one measurement (col. 1, lines 41 and 56-66) as stated in claims 30 and 61. Cabib et al. describe measuring fluorescence from various constituents including cytoplasmic proteins in the sample (col. 10, lines 57-61). Cabib et al. describe using a fluorescently labeled antibody (col. 8, lines 52-55) as stated in claim 62. Cabib et al. describe the spectral imaging enables detection at any location in the image (col. 1, lines 66-67). Cabib et al. describe spectral dispersion methods with filters which insert filters in the optical path (col. 2, line 66 to col. 3, line 13) which represents masking. Cabib et al. describe work done on imaging one or a few points of a sample (col. 3, lines 39-44). Cabib et al. describe using the system to detect differences between chemical constituents whose spatial distribution and organization is of interest along with using a filtering method such as dark field, phase contrast, and polarized light microscopy (col. 5, lines 23-45 and col. 36, lines 16-50) which represents masking. Cabib et al. describe the bio-imaging system can measure spectral differences in different parts of the cell to provide insight in to the functions of the organelles in a living cell (col. 34, lines 39-42). Cabib et al. describe identifying multiple fluorophores and using time resolved spectral imaging (col. 5, lines 46-60 and col. 8, lines 56-61). Cabib et al. describe measuring emission spectra for identifying and mapping biological components, such as proteins, within cancerous and healthy cells and tissues using various

fluorescing tags (col. 6, lines 27-53). Cabib et al. describe analyzing similarity mapping to determine differences between a sample and one or more references with color changes corresponding to the intensity of the differences (col. 9, lines 13-22 and 33-43). Cabib et al. describe a ratio of integrated intensity of spectral values or signals (col. 9, lines 28-32 and col. 10, lines 39-52). Cabib et al. describe the image of the sample is stationary on the plane of the detector array (col. 7, lines 23-36) which means the sample itself is stationary or fixed. Cabib et al. describe a signal is a particular combination of light intensity emitted by the pixel at different wavelengths and the presence and level of the signals is detected (col. 7, lines 30-36 and col. 8, lines 36-41). Cabib et al. describe recording signals as a function of time (col. 7, lines 40-43) which is reasonably interpreted to mean that measurements of light intensities are taking at multiple time points, including a first and second time point. Cabib et al. describe identifying nucleic acid probes for disease genes by marking probes with examined chromosomal regions as well as cell, tissue and gene identification and mapping (col. 5, line 61 to col. 6, line 5; col. 8, lines 47-51; and col. 10, line 62 to col. 11, line 8) which represents nucleic acid identification in cells as stated in claim 44. Cabib et al. describe displaying the bio-imaging map of the spectral cube of data (col. 7, lines 44-48). Cabib et al. describe finding which elements tag certain features in the sample (col. 9, lines 59-61). Cabib et al. describe analyzing wavelength signals from a first spectral cube of data to a second cube of data to obtain a resulting third spectral cube of data, including looking at time change follow-ups (col. 9, line 65 to col. 10, line 9). Cabib et al. describe a calibration procedure is used where the viewing is sample is divided (col. 10, lines 23-27). Cabib et al. describe the system can be used by surgeons before, during, or after surgery (col. 58, lines 22-33) which represents the use of live tissue and cells as stated in claim 65.

Cabib et al. describe classification analysis and morphological analysis involved in the spectral analysis (col. 12, lines 15-18 and 56-65). Cabib et al. also describe black and white intensity images in Figure 30 (a-c) (col. 16, lines 5-9). Cabib et al. describe chlorophyll fluorescent intensities in the cell as opposed to the cell membrane allowing the visualization of fluorescence emitted from specific subcellular regions in the cell (col. 34, line 25 to col. 35, line 13). Cabib et al. do not mention a machine readable storage medium, but do computer software and hardware and mention other existing devices may attach to the device in their invention (col. 61, lines 46-53).

Although Cabib et al. describe the above-mentioned method in a computer hardware and software program, they do not describe having this program on a machine readable storage medium using computer-executable instructions. *In re Venner* 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) states that it is obvious to computerize a manual activity. The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over prior art as stated in MPEP § 2144.04, Part III.

Cabib et al. state the widely recognized need for bio-imaging methods which provide advanced means to detect spatial organization, quantify, and display cellular components, probes, and drugs using various light and fluorescent technologies (col. 6, lines 54-62). Cabib et al. state the widely recognized need to increase objectivity and reliability of tests and to automate the prescreening stage (col. 59, lines 8-14). Cabib et al. state that other existing devices may attach to the device in their invention (col. 61, lines 46-53). A person of ordinary skill in the art would have been motivated to further develop ways of analyzing resulting signals and images

from diagnostic detection systems as stated by Cabib et al., by including these steps on a computer readable medium in order to impart understanding of the images regarding chemical, physiologic, and pathologic indications to a diagnostician, researcher, or surgeon as stated by Cabib et al. (col. 4, lines 1-4). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to place the analysis software on a machine readable storage medium for a manual activity (as discussed by *In re Venner*), because this would allow for interpretation of spectral information with present and future algorithms as well as allowing for comparisons to be made between data to enable fast and very versatile work, as stated by Cabib et al.(col. 60, last paragraph and col. 61, fourth paragraph).

Thus, Cabib et al., in view of *In re Venner*, motivate the instant invention.

Applicants state that the Patent Office bears the initial burden of establishing a prima facie case of obviousness before any rejection under 35 USC § 103 may be made. Applicants state the prior art reference must teach or suggest all of the claim limitations. This is acknowledged and the discussion above describes how the Cabib et al. reference teaches and/or suggests the instant claim limitations. Applicants have made a copy of claim 30 with bold/underlined phrases they do not believe are addressed in the Cabib et al. reference. This is found unpersuasive as the discussion above describes where in the Cabib et al. reference such bold/underlined phrases are taught or suggested. As discussed in the 35 USC § 103(a) rejection above, Cabib et al. reference does support this obviousness rejection against the instant claims which have been broadly and reasonably interpreted, including the term "masking". Applicants state Cabib does not teach or suggest providing cells that comprise a plurality of fluorescent reporter molecules that report on each of a cellular macromolecule of interest, the cell cytoplasm

and the plasma membrane. This is found unpersuasive as suggested by some of the 35 USC § 103(a) rejection passages reiterated below.

Cabib et al. describe using the method for cell and tissue classification, in drug development research as well as mapping cytoplasm organelles and constituents and the cell membrane (col. 10, line 62 to col. 11, line 12 and col. 38, line 17 to col. 39, line 9). Cabib et al. describe using the cell, tissue or organism samples to monitor life processes in the sample as a function of time (col. 11, lines 30-34). Cabib et al. describe measuring spatial separation between at least two fluorophores where one is administered to the sample (col. 11, lines 13-18). Cabib et al. describe using spectral imaging to detect proteins and nucleic acid sequences after being labeled with fluorescent probes, mapping, and sorting out several fluorophores in one measurement (col. 1, lines 41 and 56-66) as stated in claims 30 and 61. Cabib et al. describe measuring fluorescent from various constituents including cytoplasmic proteins in the sample (col. 10, lines 57-61). Cabib et al. describe using a fluorescently labeled antibody (col. 8, lines 52-55) as stated in claim 62. Cabib et al. describe identifying multiple fluorophores and using time resolved spectral imaging (col. 5, lines 46-60 and col. 8, lines 56-61). Cabib et al. describe measuring emission spectra for identifying and mapping biological components, such as proteins, within cancerous and healthy cells and tissues using various fluorescing tags (col. 6, lines 27-53). Cabib et al. describe chlorophyll fluorescent intensities in the cell as opposed to the cell membrane allowing the visualization of fluorescence emitted from specific subcellular regions in the cell (col. 34, line 25 to col. 35, line 13).

Applicants submit the prior art does not teach creating masks, determining intensities of fluorescent signals within the masks, comparing intensities in treated versus non-treated cells, or using these comparisons to determine effect of test compounds on the distribution of the cellular macromolecule of interest between the plasma membrane and the cytoplasm in individual cells. This submission is found unpersuasive as Cabib et al. addresses what is recited in the instant claims that were broadly and reasonably interpreted. As stated above, Cabib et al. discuss masking in the following passages:

Cabib et al. describe spectral dispersion methods with filters which insert filters in the optical path (col. 2, line 66 to col. 3, line 13) which represents masking. Cabib et al. describe work done on imaging one or a few points of a sample (col. 3, lines 39-44). Cabib et al. describe using the system to detect differences between chemical constituents whose spatial distribution and organization is of interest along with using a filtering method such as dark field, phase contrast,

and polarized light microscopy (col. 5, lines 23-45 and col. 36, lines 16-50) which represents masking.

Cabib et al. discuss determining intensities, including within treated versus non-treated cells in the following passages:

Cabib et al. describe bio-imaging methods involving measurements and analysis software that detect spatial organization, such as distribution, and quantify cellular constituents, structures, organelles and administered components such as tagged fluorescent probes and drugs (test stimulus) using light transmission, reflection, scattering, and fluorescence emission strategies (col. 1, lines 13-25 and col. 2, lines 3-4). Cabib et al. describe measuring spatial separation between at least two fluorophores where one is administered to the sample (col. 11, lines 13-18). Cabib et al. describe measuring emission spectra for identifying and mapping biological components, such as proteins, within cancerous and healthy cells and tissues using various fluorescing tags (col. 6, lines 27-53). Cabib et al. describe analyzing similarity mapping to determine differences between a sample and one or more references with color changes corresponding to the intensity of the differences (col. 9, lines 13-22 and 33-43). Cabib et al. describe a ratio of integrated intensity of spectral values or signals (col. 9, lines 28-32 and col. 10, lines 39-52). Cabib et al. describe a signal is a particular combination of light intensity emitted by the pixel at different wavelengths and the presence and level of the signals is detected (col. 7, lines 30-36 and col. 8, lines 36-41). Cabib et al. also describe black and white intensity images in Figure 30 (a-c) (col. 16, lines 5-9). Cabib et al. describe chlorophyll fluorescent intensities in the cell as opposed to the cell membrane allowing the visualization of fluorescence emitted from specific subcellular regions in the cell (col. 34, line 25 to col. 35, line 13).

Cabib et al. describe determining effect of test compounds on the distribution of the cellular macromolecule of interest between the plasma membrane and the cytoplasm as described below:

Cabib et al. describe bio-imaging methods involving measurements and analysis software that detect spatial organization, such as distribution, and quantify cellular constituents, structures, organelles and administered components such as tagged fluorescent probes and drugs (test stimulus) using light transmission, reflection, scattering, and fluorescence emission strategies (col. 1, lines 13-25 and col. 2, lines 3-4). Cabib et al. describe using the method for cell and tissue classification, in drug development research as well as mapping cytoplasm organelles and constituents and the cell membrane (col. 10, line 62 to col. 11, line 12 and col. 38, line 17 to col. 39, line 9). Cabib et al. describe algorithms to interpret spectral information of chemical elements (concentration mapping) and/or morphological interpretation using image shapes (col. 61, lines 33-45). Cabib et al. describe using the cell, tissue or organism samples to monitor life processes in the sample as a function of time (col. 11, lines 30-34).

Applicants' arguments are deemed unpersuasive, and the 35 USC § 103(a) rejection has been maintained.

The effective filing date for claims including the phrase "cell membrane" is the actual filing date of this application (11/27/00) as no mention of "cell membrane" appears in the priority documents.

The rejection of claims 30, 44, 54, and 61-65 is maintained under 35 U.S.C. 103(a) as being unpatentable over Harris et al. (P/N 6,388,788) in view of *In re Venner*.

This rejection is reiterated and maintained for reasons of record.

Harris et al. describe a method and apparatus for screening pharmaceutical compounds in fluorescent assays, including live cell assays (abstract). Harris et al. describe analyzing images to determine the amount of a first fluorescently labeled species localized compared to a second fluorescently labeled species (col. 25, lines 49-54) which is a form of distribution detection. Harris et al. describe the method involving real time data-processing at video rates (abstract). Harris et al. disclose screening proteins (col. 1, lines 44-56). Harris et al. describe using fluorescent dyes applied to cells on the bottom of the wells of a multi-well plate and scanning the sample which remains at a fixed position (col. 1, lines 60-67; col. 6, lines 45-57; and col. 7, lines 38-40 and 54-61). Harris et al. describe using a multi-parameter fluorescence imaging on single cells and cell populations (col. 2, lines 53-56). Harris et al. describe the ability to determine the locations of the multiple fluorophores with sub-cellular resolution (col. 2, lines 60-61). Harris et al. describe the target of interest may be in a cell, subcellular organelle, or on the cell membrane (col. 7, lines 7-10). Harris et al. describe translocation assays with two or more fluorescently-labeled species, such as proteins, from one well-defined region of the cell to another (col. 26, line

63 to col. 27, line 7). Harris et al. describe comparing first and second species co-localized and various ratios among them (col. 27, lines 8-15). Harris et al. describe labeling the cell nucleus with a label being a fluorophore specific for DNA (col. 27, lines 16-20). Harris et al. describe determining the amount of a first and second fluorescently labeled species to determine the activity of a compound (col. 27, lines 28-34). Harris et al. describe the use of various binary masks, including one for cytoplasmic intensity in Figures 20A-D. Harris et al. describe determining fluorescent intensities (col. 27, lines 28-34), using a binary mask (col. 27, lines 56-58), searching the bitmap for objects (col. 27, lines 58-67), and continuing analysis on objects passing the filter criteria to calculate intensities of the objects associated with a particular mask (col. 28, lines 1-34). Harris et al. describe creating annular masks (col. 28, lines 15-34) which can reasonably be interpreted to form for objects such as the cell membrane. Harris et al. describe calculating the ratio of eroded annular intensities for each object and determining average intensities as well as comparing ratio fractions for the fluorescently-labeled species (col. 26, lines 46-51). Harris et al. describe creating two daughter masks, one being an annular extension of a primary mask and one being an eroded version of the primary mask for a cell (col. 28, lines 38-47) which is reasonably interpreted to include a cell membrane mask and a cytoplasmic mask. Harris et al. describe creating ratios of the quantities on a cell-by-cell basis (col. 28, lines 44-47). Harris et al. describe determining the location and intensities of the multiple fluorescently labeled species as well as their correlations (col. 7, lines 11-19). Harris et al. describe performing the imaging at a single or multiple time points (col. 7, lines 19-27). Harris et al. describe acquiring data on individual cells to constitute data for a cell population (col. 9, lines 20-25). Harris et al. describe using fluorescently labeled antibodies (col. 20, line 29

and col. 27, lines 23-27). Harris et al. describe using membranes from cells in a receptor-binding assay using fluorescent labels (col. 20, line 48 to col. 21, line 49). Harris et al. describe comparing images from wells containing a test compound to control wells (col. 21, lines 50-56). Harris et al. describe a fluorescence signal of interest might originate from the receptor in the nucleus (col. 23, lines 26-29) which is a form of identification as stated in claim 44. Harris et al. describe identifying an object to which fluorescently labeled species bind (col. 25, lines 43-56 and col. 26, lines 52-61).

Although Harris et al. describe the above-mentioned method computing device, they do not describe having this program on a machine readable storage medium using computer-executable instructions. *In re Venner* 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958) states that it is obvious to computerize a manual activity. The court held that broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over prior art as stated in MPEP § 2144.04, Part III.

A person of ordinary skill in the art would have been motivated to enhance the procedures of detecting distribution of cellular components, as stated by Harris et al., by including these steps on a computer readable medium in order to quickly screen a large number of compounds, as stated by Harris et al. (col. 1, lines 44-45). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to place method and apparatus instructions including data processing routines (Harris et al., col. 1, lines 15-22) on a machine readable storage medium for a manual activity (as discussed by *In re Venner*) such as basic identification of cellular component distribution in cells (as stated by Harris et al), because this information would enhance and quicken access to the identification of

compounds to be used as pharmaceutical agents, as stated by Harris et al. (col. 1, lines 15-22 and 44-45 and col. 2, lines 53-65).

Thus, Harris et al., in view of *In re Venner*, motivate the instant invention.

Applicants state the amended claims recite "plasma membrane" which is known by those of skill in the art to be synonymous with "cell membrane" and that the present specification is identical to US application 09/031,271 that provides support for "plasma membrane". This amended material is considered NEW MATTER (see 35 USC 112, first paragraph rejection above) that should be deleted from the claims and therefore does not get the priority date requested. The 35 USC 103(a) rejection including the Harris et al. reference is therefore maintained.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

March 23, 2004

Ardin H. Marschel 4/1/04
ARDIN H. MARSCHEL
PRIMARY EXAMINER